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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,291	10/14/2005	Mary J. Eaton	US 1442/05(VA)	8630

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EXAMINER	
GAMETT, DANIEL C	
ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
09/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,291	EATON, MARY J.	
	Examiner	Art Unit	
	DANIEL C. GAMETT	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06/09/2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,9,15,16,28,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *2,4,9 and 28* is/are allowed.

6)☒ Claim(s) *15,16,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/09/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendments of 06/09/2008 have been entered in full. Claims 1, 3, 5-8, 10-14, 17-27, and 29 are cancelled. Claims 2, 4, 9, 15, 16, 28, and 30, and 31 are under examination.

2. All prior objection/rejections not specifically maintained in this office action are hereby withdrawn.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 15, 16, 30, and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods for treating spasticity and pain following spinal cord injury and for neurological disorders known to be characterized by low levels of GABA and amenable to cell transplantation therapy, comprising transplanting GABA expressing, cloned hNT2 cells, does not reasonably provide enablement for treatment of all neurological diseases, conditions, or disorders by administering GABA expressing, cloned hNT2 cells to all sites in or adjacent to the central or peripheral nervous system. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

5. The methods of claims 30 and 31, and the intended use of the composition of claims 15 and 16 are not limited to any particular disease, but instead they recite any "neurological disease, condition, or disorder". The claimed methods, therefore, encompass treatment of diseases that the currently lack effective treatments, such as brain tumors and neurodegenerative diseases, as well as conditions for which there is no reason to believe that implantation of GABA producing cells would be beneficial. Reviews published after the priority date of the instant application indicate that cell transplantation for the treatment of neurological conditions is a highly complex art and that results are unpredictable. Lindvall et al., *Nature Medicine* 10, S42-S50 (2004), for example, point out that, in each disease, a different spectrum of cell types is affected (Lindvall et al., page S42, left column). Similarly, Isacson (*Lancet Neurology* 2003; **2:** 417–224) indicates that "neurological disorders caused by acute and widespread damage, such as spinal-cord injury and stroke, present a substantial conceptual and therapeutic challenge: transplantation of many different cell types would be required to reconstitute tissue after these sorts of injuries" (Isacson, p.422, right column). Conditions where a single neuronal type is primarily effected are better candidates for cell therapy, but successful treatment is not predictable even when transplanted cells survive. Regarding Parkinson's disease, for example, Lindvall *et al.* indicate that "it remains to be shown that the stem cell-derived neurons, after implantation in animal models, fulfill the requirements of successful graft-that is, to reinnervate most of the of the denervated striatum, restore dopamine release in vivo and substantially improve Parkinson's-like symptoms" (Lindvall et al., page S43, left column). For ALS, recent findings support the "strategy of differentiating stem cells along specific cortical neuronal lineages *in vitro* and transplanting

them so as to reconstruct cortical circuitry" Further, "it is unknown, though, if such cortical neuronal replacement will work in the brains of individuals with ALS" (Lindvall et al., page 548, left column).

6. Enablement must be provided by the specification unless it is well known in the art. *In re Buchner* 18 USPQ 2d 1331 (Fed. Cir. 1991). The specification provides examples of animal models relevant to pain and spasticity, wherein rats were given subarachnoid transplants of the disclosed cells after spinal cord injury induced by spinal transaction or an excitoxic agent.

7. The state of the art indicates a few limited examples of therapeutic administration of GABA-expressing neurons. With regard to epilepsy, the art teaches that local application of GABA-potentiating agents can prevent or reduce the development and maintenance of behavioral seizures induced by limbic kindling in rats and that this effect can be achieved by transplantation of genetically engineered GABA producing cells (Gernert et al., Experimental Neurology, Volume 176, Issue 1, July 2002, Pages 183-192, see Abstract and cited references). A demonstration that implantation of engineered GABA-releasing cells into substantia nigra reduced tremulous movements in an animal model of parkinsonian tremor occurred almost simultaneously with the instant application (Carlson et al., *Neuroscience* 119 (16 July, 2003) 927–932). Grafted populations of comprising GABAergic and glutamatergic neurons derived from pluripotent NT2 cells have been shown to restore function in an animal model of spinal cord injury (US 6214334, April 10, 2001, of record; see Example 5 for neurotransmitter types, and Example 7 for graft results). GABAergic neurons in the striatum degenerate in Huntington's disease (Isacson, p.420-421; Fig. 3). US Patent 6254865 (Freed),

July 3, 2001 (of record) teaches improvement of motor skills in by administration of hNT neurons into the striatum in animal models of Huntington's disease.

8. The prior art provides no examples of attempted alleviation of symptoms of Alzheimer's disease or depression by transplantation of GABA expressing neurons. Indeed, while neurotransmitter imbalances are likely to underlie the symptoms of most, if not all, neurological diseases, a specific role for GABA, such that administration of GABA producing cells would be predictably beneficial, has not been established across the entire scope of diseases encompassed by the claims.

9. Due to the complex nature of the invention and the state of the prior art, which established the unpredictability and limited efficacy of cell-based therapies for neurological disease even when replacement of only a single type is desired, the lack of direction/guidance presented in the specification regarding implantation of cells to sites other than subarachnoid transplants, or for the treatment of conditions other than spinal cord injuries, the absence of working examples directed to same, and the breadth of the claims which encompass all neurological diseases, conditions, and disorders, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

10. Claims 2, 4, 9, and 28 are allowable.

11. Claims 15, 16, 30, and 31 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C. Gamett, PhD., whose telephone number is (571)272-1853. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on 571 272 0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DCG
Art Unit 1647

/David S Romeo/
Primary Examiner, Art Unit 1647